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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/251,073 | 02/16/1999 | ROY R. LOBB | 10274-003003 | 2802 |

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|---|---|
| GAMBEL, PHILLIP | |
| **ART UNIT** | **PAPER NUMBER** |
| 1644 | 16 |

DATE MAILED: 07/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

BEST AVAILABLE COPY

| Office Action Summary | Application No. 09/251073 | Applicant(s) LOBB |
|---|---|---|
| | Examiner GAMBEL | Art Unit 1644 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☑ Responsive to communication(s) filed on 1/23/02; 5/13/02

2a)☐ This action is **FINAL**. 2b)☑ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☑ Claim(s) _____ is/are pending in the application. 1-3, 6, 7, 9-13, 17, 18, 26-37

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 1-3, 6, 7, 9-13, 17, 18, 26-37

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☑ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☑ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☑ Notice of References Cited (PTO-892)
2) ☑ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

1. Applicant's Sequence Submission, filed 5/13/02 (Paper No. 14), has placed this application in compliance with the Sequence Rules.

Applicant is required to amend the specification and the claims (see claims 13 and 26) to indicate the appropriate SEQ ID NOS.

2. The following is of record.
Applicant's amendment, filed 1/23/02 (Paper No. 12), has been entered.
Claims 4, 5, 8, 14-16 and 19-25 have been canceled.
Claims 1-3, 6, 7, 9, 11-13 and 17-18 have been amended.
Claims 26-37 have been added.

Applicant's election without traverse of Group I as it reads on treating asthma with fibronectin polypeptide in Paper No. 12 is acknowledged.

Claims 1-3, 6, 7, 9-13, 17, 18 and 26-37 are pending and under consideration.

3. The filing date of the instant claims is deemed to be the filing date of the priority application USSN 08/456,193, filed 5/31/95, as the previous priority applications do not provide sufficient written description for treating asthma with fibronectin and fibronectin-derived peptides encompassing the claimed limitations of the instant application.

If applicant desires priority prior to 5/31/95; applicant is invited to point out and provide documentary support for the priority of the instant claims. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

4. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Applicant should amend the first line of the specification to update the status (and relationship) of the priority documents, including USSN 08/822,830 and 08/456,193.
Also, given the priority issues concerning the instant claims as set forth above in Section 3, applicant is invited to reconsider the priority claimed on the first line of the specification.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

6. The Abstract of the Disclosure is objected to because it does not adequately describe the claimed invention. Correction is required. See MPEP 608.01(b).

7. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

Applicant is reminded to change the Brief Description of the Drawings in accordance with these changes, if appropriate.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in ABANDONMENT of the application.

8. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined *under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e))*.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-3,10, 26 and 27 are rejected under 35 U.S.C. § 102(e) as being anticipated by Wayner et al. (U.S. Patent No. 5,730,978) (see entire document).

Wayner et al. teach methods of suppressing the immune response in human patients, including chronic and relapsing inflammation, including asthma by interfering the binding of receptor-ligand interactions between lymphocytes and endothelial cells (see Utility of the Invention, columns 15-17, including column 16, paragraph 1). Here, the inhibitory peptides may be administered by any route, including intravenously, intranasal and oral (column 16, paragraph 2 - column 17, paragraph 1). Wayner et al. teach that the inhibitory peptide comprising fibronectin, a portion of fibronectin including the fibronectin alternatively spliced IIICS region including the CS-1 domain comprising the EILDV motif which block adhesive events, including those with $\alpha 4\beta 1$ expressing lymphocytes and endothelial cells (see entire document, including Fibronectin, columns 3-7; Summary of the Invention, column 7-8; Detailed Description of the Invention, including columns 10 - 17 and Examples. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to treat asthma with fibronectin and fibronectin peptides that block lymphocyte-endothelial interactions.

12. Claim 1-3,10, 26 and 27 are rejected under 35 U.S.C. § 102(e) as being anticipated by Kogan et al. (U.S. Patent No. 5,510,332) (see entire document).

Kogan et al. teach methods of treating diseases associated with uncontrolled migration of white blood cells to damaged tissues such as asthma by inhibiting the binding of $\alpha 4\beta 1$ to VCAM-1 and that means for determining effecting inhibiting amounts are well known in the art (see Process of Inhibiting the Binding of $\alpha 4\beta 1$ Integrin to VCAM-1, columns 9-10). Here, the pharmaceutical compositions can be administered to humans by intravenous injection of intranasally via a spray or aerosol (see Pharmaceutical Composition; columns 8-9). Kogan et al. teach that $\alpha 4\beta 1$ recognizes fibronectin, including fibronectin isoforms including the CS1 peptide present in the alternatively spliced type III connecting segments (see Detailed Description of the Invention, including The Invention on column 3 and Peptides on columns 3-8 and Examples, including SEQ ID NO: 101). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to treat asthma with fibronectin and fibronectin peptides that block lymphocyte-endothelial interactions

13. Claim 1-3,6, 7, 10, 26 and 27 are rejected under 35 U.S.C. § 102(e) as being anticipated by Arrhenius et al. (U.S. Patent No. 6,117,840) (see entire document).

Arrhenius et al. teach methods of blocking interactions between the fibronectin peptide CS-1 and VLA-4 (i.e. $\alpha 4\beta 1$) to inhibit inflammatory responses, including asthma, asthmatic lung (see Compositions and Process, columns 24-28). Here, the pharmaceutical compositions are administered in the manner of administration of the particular disease being treated and its severity, including parenteral and local administration such as aerosol in amounts of about 0.25 mg to about 25 mg and about 1 mg/kg/day to about 500 mg/mg/kg/day of the inhibitor peptide, including prophylactically treating patients at risk (see columns 25-28). Arrhenius et al. teach the use of fibronectin and fibronectin derived peptides such as CS-1 and SEQ ID NO: 3 to block various inflammatory conditions by blocking blocking interactions between the fibronectin peptide CS-1 and VLA-4 (i.e. $\alpha 4\beta 1$) (see entire document, including Background of the Invention, Summary of the Invention and Detailed Description of the Invention). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to treat asthma with fibronectin and fibronectin peptides that block lymphocyte-endothelial interactions.

14. Claims 1-3, 6, 7, 9-13, 17, 18 and 26-37 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Wayner et al. (U.S. Patent No. 5,730,978) AND/OR Kogan et al. (U.S. Patent No. 5,510,332) AND/OR Arrhenius et al. (U.S. Patent No. 6,117,840) in view of art known of the nature and treatment of asthma at the time the invention was made as acknowledged in the Background of the Invention on pages 1-3 of the instant specification and pages 7-8 of the instant specification.

Wayner et al. teach methods of suppressing the immune response in human patients, including chronic and relapsing inflammation, including asthma by interfering the binding of receptor-ligand interactions between lymphocytes and endothelial cells (see Utility of the Invention, columns 15-17, including column 16, paragraph 1). Here, the inhibitory peptides may be administered by any route, including intravenously, intranasal and oral (column 16, paragraph 2 - column 17, paragraph 1). Wayner et al. teach that the inhibitory peptide comprising fibronectin, a portion of fibronectin including the fibronectin alternatively spliced IIICS region including the CS-1 domain comprising the EILDV motif which block adhesive events, including those with $\alpha 4\beta 1$ expressing lymphocytes and endothelial cells (see entire document, including Fibronectin, columns 3-7; Summary of the Invention, column 7-8; Detailed Description of the Invention, including columns 10 - 17 and Examples.

Kogan et al. teach methods of treating diseases associated with uncontrolled migration of white blood cells to damaged tissues such as asthma by inhibiting the binding of $\alpha 4\beta 1$ to VCAM-1 and that means for determining effecting inhibiting amounts are well known in the art (see Process of Inhibiting the Binding of $\alpha 4\beta 1$ Integrin to VCAM-1, columns 9-10). Here, the pharmaceutical compositions can be administered to humans by intravenous injection of intranasally via a spray or aerosol (see Pharmaceutical Composition; columns 8-9). Kogan et al. teach that $\alpha 4\beta 1$ recognizes fibronectin, including fibronectin isoforms including the CS1 peptide present in the alternatively spliced type III connecting segments (see Detailed Description of the Invention, including The Invention on column 3 and Peptides on columns 3-8 and Examples, including SEQ ID NO: 101)

Arrhenius et al. teach methods of blocking interactions between the fibronectin peptide CS-1 and VLA-4 (i.e. $\alpha 4\beta 1$) to inhibit inflammatory responses, including asthma, asthmatic lung (see Compositions and Process, columns 24-28). Here, the pharmaceutical compositions are administered in the manner of administration of the particular disease being treated and its severity, including parenteral and local administration such as aerosol in amounts of about 0.25 mg to about 25 mg and about 1 mg/kg/day to about 500 mg/mg/kg/day of the inhibitor peptide, including prophylactically treating patients at risk (see columns 25-28). Arrhenius et al. teach the use of fibronectin and fibronectin derived peptides such as CS-1 and SEQ ID NO: 3 to block various inflammatory conditions by blocking blocking interactions between the fibronectin peptide CS-1 and VLA-4 (i.e. $\alpha 4\beta 1$) (see entire document, including Background of the Invention, Summary of the Invention and Detailed Description of the Invention).

Wayner et al., Kogan et al. and/or Arrhenius et al differ from the claimed methods by not explicitly disclosing the art known course and types of asthma as well as the art known practice to treat asthma prior and after allergen exposure and early and late phase and such patients are considered hypersensitive by one of ordinary skill in the art at the time the invention was made.

The Background of the Invention (pages 1-3 of the instant specification) discloses the art known natural history of asthma, including the role of allergens in airway inflammation as well as early and late phase responses in allergen-induced asthma, wherein such patients are considered hypersensitive and discloses the art known of drugs to treat asthma by blocking or neutralizing the effects of inflammatory mediators before, during and after these responses.

Pages 7-8 of the instant specification discloses that the modes of administration and the effective dosages of inhibitors were familiar to physicians experienced in the treatment of allergic asthma, which depends on the patient and on the course of the disease.

Given the well known practices of the ordinary artisan in the treatment of asthma, including allergen-induced asthma at the time the invention, which is consistent with the treatment of asthma of fibronectin-derived inhibitors which block the interactions between $\alpha 4\beta 1$ and its receptor between lymphocytes and endothelial cells in order to inhibit inflammatory responses as taught by Wayner et al., Kogan et al. and/or Arrhenius et al. These references are consistent with the acknowledged art in the instant specification as filed that effective dosages of inhibitors are provided in the manner of administration of the particular disease being treated and its severity and the patient's needs, including intravenous and aerosol over a broad range of dosages.

One of ordinary skill in the art at the time the invention was made would have been motivated to select fibronectin-derived peptides, including those comprising EIDLV to treat asthma, including allergen-induced asthma by inhibiting the interaction between lymphocytes and endothelial cells. Given the art known course and treatment of asthma which undergoes acute and chronic phases in responses to allergens, one of ordinary skill in the art would have been motivated to treat asthmatic patients prior to, during and after allergen exposure with the dosages encompassed by the claimed invention. It was routine for the ordinary artisan in asthma would have manipulated the appropriate dosings and modes of administrations to meet the needs of the patients and the course of the disease at the time the invention was made. The claimed timing of administration and effective dosages were well known in the art, as the ordinary artisan would have applied fibronectin inhibitors to achieve the therapeutic endpoint of diminishing inflammatory conditions in asthmatic patients, including allergen-induced asthmatics. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
July 24, 2002